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CASE 4-30028/A/PCT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE PCT NATIONAL STAGE APPLICATION OF
PORTMANN ET AL.
INTERNATIONAL APPLICATION NO: PCT/EP 98/03427
FILED: 8 JUNE 1998
U.S. APPLICATION NO: 09/125,329
35 USC §371 DATE: 8 SEPTEMBER 1998
FOR: CRYSTAL MODIFICATION OF 1-(2,6-DIFLUOROBENZYL)-1H-1,2,3-TRIAZOLE-4-CARBOXAMIDE AND ITS USE AS ANTIEPILEPTIC

Art Unit: 1625
Examiner: P. Morris

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY BRIEF

Sir:

This is in reply to the Examiner's Answer dated June 20, 2001.

Appellants acknowledge the Examiner's withdrawal of: 1) the rejection of all of the claims on appeal under 35 U.S.C.§102(a), (b), (e) and/or (f) as being anticipated by Meier I and Meier II; and 2) the rejection of all of the claims on appeal under the second paragraph of 35 U.S.C.§112 as being indefinite.

As to the rejections which remain on appeal, the Examiner has again maintained the rejection of all of the claims on appeal under 35 U.S.C.§103(a) as being unpatentable over Meier I and Meier II in view of Munzel I and Munzel II. The Examiner again contends that since the Meier references disclose a crystalline form of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, save for the lines with interplanar spacings of the X-ray powder pattern of said form or any other characterizing parameters, and since the Munzel references teach that compounds can exist in different polymorphic forms which retain the activity of the compounds, the crystalline

forms of the appealed claims would have been *prima facie* obvious to one skilled in the art from the combined teachings of the references.

In addition, the Examiner has again maintained the rejection of all of the claims on appeal under the judicially created doctrine of "obviousness-type double patenting" as being unpatentable over Claims 1-10, 14 and 20 of USP 4,789,680 (Meier II) in view of Munzel I and II. The Examiner again contends that since Meier II discloses a crystalline form of the compound (1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide and since the Munzel references teach that compounds can exist in different polymorphic forms, the appealed claims are not patentably distinct over certain of the claims in USP 4,789,680.

Moreover, the Examiner has again maintained the rejection of all of the claims on appeal under the judicially created doctrine of "obviousness-type double patenting" as being unpatentable over the claims of co-pending U.S. Application No. 09/599,688 in view of Munzel I and II. The Examiner again contends that since co-pending U.S. Application No. 09/599,688 discloses a crystalline form of the compound (1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, viz., crystal modification B, and since the Munzel references teach that compounds can exist in different polymorphic forms, the appealed claims are not patentably distinct over the claims in co-pending U.S. Application No. 09/599,688.

Furthermore, the Examiner has made some ancillary comments concerning the Appeal Brief. More particularly, the Examiner has criticized Documents 1 and 2 because: 1) they were not submitted earlier; 2) they are in German; and 3) they are devoid of any surprising and unexpected results for the claimed crystalline forms.

Still further, the Examiner has cited "new" case law to support her position regarding the "obviousness" rejection, viz., Glaxo Inc. v. Novopharma Ltd., 34 USPQ 2d, 1565. It is the Examiner's contention that the dicta of the court intimates that "new" crystalline forms are *prima facie* obvious and that the submission of unexpected and surprising evidence is necessary to obtain the allowance of claims thereto.

Appellants' position with regard to the "obviousness" rejection and the two "obviousness-type double patenting" rejections is believed to be adequately set forth in the Appeal Brief and, therefore, will not be set forth in detail herein to avoid an unnecessary lengthening of the record.

In brief and with regard to the "obviousness" rejection, there must be a suggestion or teaching in the prior art that the "new" crystalline forms discovered by the Appellants could or

should be made, whether by manipulation of the prior art process being relied upon or by some other process. Clearly, there is nothing in the combined teachings of the Meier and Munzel references or any other prior art which would suggest or teach that crystalline forms of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide exist and that they could or should be made. Nor, more importantly, is there anything in the combined teachings of the Meier and Munzel references or any other prior art which would suggest or teach a method of making the crystalline forms of the appealed claims. Therefore, it is Appellants' belief that the crystalline forms of the appealed claims are unobvious and patentable over the combined teachings of the Meier and Munzel references.

In addition, it is clear that there is nothing in the combined teachings of the Meier and Munzel references which would provide one skilled in the art with the motivation to prepare the pharmaceutical compositions of appealed Claims 26 and 28. Since the crystalline forms of the claimed pharmaceutical compositions are novel and unobvious, the claimed pharmaceutical compositions are novel and unobvious.

Similarly, and with regard to the first "obviousness-type double patenting" rejection, since there is nothing in the combined teachings of the Meier II and the Munzel references which would suggest or teach that crystalline forms of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide exist and that they could or should be made or which would suggest or teach a method of making Appellants' claimed crystalline forms, it is Appellants belief that the appealed claims are patentably distinct over certain of the claims in Meier II.

With regard to the second "obviousness-type double patenting" rejection, although co-pending U.S. Application No. 09/599,688 claims crystal modifications B and C and additionally mentions the existence of crystal modifications A and A', i.e., the two crystalline forms to which the appealed claims are directed, co-pending U.S. Application No. 09/599,688 is silent with regard to any teachings as to how the specific crystalline forms of the appealed claims can be prepared and the Munzel references do not cure this defect. Therefore, it is Appellants' belief that the appealed claims are patentably distinct over the claims in co-pending U.S. Application No. 09/599,688.

Turning to the Examiner's ancillary comments concerning the Appeal Brief and, more particularly, the Examiner's criticisms relating to Documents 1 and 2, Appellants respectfully submit that Documents 1 and 2 were not made of record earlier because it was not believed that the Examiner had established a *prima facie* case of obviousness in the Official Action dated June 1, 2000, i.e., it was not believed that the combined teachings of the Meier and Munzel references rendered any of the claims presently under appeal *prima facie* obvious. Thus, Appellants were

quite confident that their arguments responsive to the "obviousness" rejection in the Official Action dated June 1, 2000 would persuade the Examiner to reconsider and withdraw the rejection. However, since the Examiner remained adamant and maintained the "obviousness" rejection in the Final Rejection dated October 13, 2000, Documents 1 and 2 were submitted in order to dispel any lingering doubts that the Examiner may have had regarding the deficiency of the teachings of the Meier references to the crystalline forms to which the claims presently under appeal are directed.

Admittedly, Documents 1 and 2 are in German. However, Appellants did not see the need to translate Documents 1 and 2 in their entirety because of the prohibitive cost involved in obtaining English translations of foreign language technical documents, and especially because the major portions of the disclosure in Documents 1 and 2 are not relevant to the question of "patentability". Ergo, only the salient passages relevant to patentability were translated into English.

That Documents 1 and 2 are devoid of evidence demonstrating unexpected superiority is an unarguable assertion of fact with which Appellants will not quibble. However, Appellants respectfully submit that patentability in this case is not dependent on such evidence. Unexpected superiority is relevant where a case of *prima facie* obviousness has been established and rebuttal by Applicants is required. The Patent and Trademark Office has the burden of establishing the prima facie case of obviousness by showing that some objective teachings in the prior art or knowledge generally available provides a clear suggestion of the invention and a method of carrying it out. In the "obviousness" rejection presently under appeal, the Patent and Trademark Office has not met this burden. There is no objective teaching in either of the Meier references which could be said to clearly suggest the existence of Appellants' claimed crystalline forms and certainly nothing which would suggest how they can be obtained. Although the synthesis described in Example 35 of the Meier II reference results in the obtainment of 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide in solid form, the description is devoid of any mention of any crystal modification or mixture thereof. In fact, upon reproducing the example, one skilled in the art would still be unaware of the existence of crystalline forms or how they can be obtained since the crystallization conditions (e.g., concentration, quality of the solvent, quality of the crude product, temperatures, type of crystallization such as seeding, change in temperatures, etc.) are absent. In addition, from the melting point set forth in Example 35 of the Meier II reference, no definitive conclusion can be drawn that any crystalline form was present at room temperature since, by heating, a transformation can take place. Therefore, the mere indication of the temperature does not allow for any characterization of the solid product obtained. Still further, it is not even possible to presume which crystalline form has actually melted.

In any event, the submission of Documents 1 and 2 was intended to show that more than three years later than the filing date of USP 4,789,680 (aka, the Meier II reference), the sole patentee of the two Meier references relied upon by the Examiner, viz., René Meier, not only doubted that CGP 33101 (aka, Example 4 of Meier I and Example 35 of Meier II) existed in different polymorphic forms, but was not motivated to investigate the "polymorphism" aspect of CGP 33101.

With regard to the Examiner's reliance on Glaxo Inc. v. Novopharma Ltd. in an apparent effort to support her position, a review of this case failed to uncover anything which intimates that "new" crystalline forms are *prima facie* obvious and that the submission of unexpected and surprising evidence is necessary to obtain the allowance of claims thereto. As indicated above, unexpected superiority is relevant where a case of *prima facie* obviousness has been established and, in the "obviousness" rejection presently under appeal, the Patent and Trademark Office has not met this burden. Quite simply, there is nothing in either of the Meier references relied upon by the Examiner which could be said to clearly suggest the existence of Appellants claimed crystalline forms and certainly nothing which would suggest how they can be obtained.

In summation, for the reasons set forth herein and in the Appeal Brief of record, none of the claims on appeal, i.e., Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31; 1) is rendered *prima facie* obvious over the combined teachings of the Meier and Munzel references; 2) is patentably indistinct over certain of the claims in Meier II; and 3) is patentably indistinct over the claims in co-pending U.S. Application No. 09/599,688.

In accordance with 37 CFR 1.193(b), two additional copies of this Reply Brief are submitted herewith.

Respectfully submitted,

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Encls.: Two additional copes of Reply Brief

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